D.31. Jerry W. King

Jerry W. King was born on February 19, 1942, in Indianapolis, IN. He graduated from Butler University in 1965, with a B.Sc. in Chemistry. J.W. King continued with graduate studies at Butler University and the University of Utah, where he worked with J. Calvin Giddings on supercritical-fluid chromatography. In 1973, J.W. King received his Ph.D. from Northeastern University in Boston, MA under the direction of Barry Karger. He then conducted postdoctoral research in physical chemistry under Dan Martire at Georgetown University in Washington, DC.

J.W. King has worked with several industrial companies and R&D organizations prior to his appointment as a research scientist at USDA (United States Department of Agriculture). These have included Arthur D. Little, Inc. (Cambridge, MA), Union Carbide Corporation (Bound Brook, NJ), and CPC International (Summit-Argo, IL). While at CPC he was in charge of HPLC methods development for biotechnology, installation of a process monitoring HPLC in the pilot plant, and industrial products analysis.

Since 1988, he has been the Lead Scientist of the Critical Fluid Technology Group at the National Center for Agricultural Utilization Research (NCAUR) in Peoria, IL. His research interests there have included the development of critical fluid technology for food and agrimaterial processing, as well as for the analysis of toxicants, nutrients, and fats/oils. He has authored over 125 publications (including two patents) in SFE (supercritical-fluid extraction), SFC (supercritical-fluid chromatography), and related separation techniques, and has lectured extensively on these subjects over the past 14 years at national and international symposia, including the ACS Shortcourse on SFE/SFF/SFC with Larry Taylor. J.W. King has organized many symposia on SFE and SFC, including the well-known International Symposia on SFC and SFE. He serves on the Editorial Board of the Journal of Supercritical Fluids, Italian Journal of Food Science, Seminars in Food Science and is a member of the American Chemical Society (ACS), American Oil Chemists Society (AOCS), Institute of Food Technology (ITF), Association of Official Analytical Chemists (AOAC), and regional/international supercritical fluid technology groups.

In 1993, J.W. King was named Scientist of the Year at NCAUR, and in 1994 was elected a corresponding member of the Academia dei Georgofili in Florence, Italy. J.W. King has been awarded the Chicago Chromatography Discussion Group's Merit Award for significant contributions to chromatography and was elected to Who's Who in America. He was awarded the Harvey Wiley Award of the AOAC in 1997 for his research in analytical SFE. In 1998, received the Merit Award from the Midwest SFC Group/Tri-State Discussion Group for consistent contributions in the supercritical fluid technology field, and the Award of Excellence at the 8th International Symposium on SFC/SFE for pioneering achievement, leadership, and enthusiasm in the development of supercritical fluid technology and the education of others. In 2000, he received the Keene P. Dimick Award for his contributions to the field of gas and supercritical-fluid chromatography.

See Chapter 5B, a, d, h, o, s

31.I. THE USE OF SUPERCRITICAL FLUIDS IN ANALYTICAL CHEMISTRY

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My first initiation into the realm of supercritical fluid technology occurred in 1967 when I was considering at which university I should continue my graduate studies. Reading a publication by J. Calvin Giddings sparked my interest in the University of Utah and I subsequently visited Cal that summer to find out more about this interesting topic. Late in the summer of 1968, I migrated to Salt Lake City and began research in this area, which would later become the focal point of my research career. Supercritical-fluid chromatography (SFC) in those days went under the titles as 'dense phase gas chromatography'. Giddings' research group at Utah was laying the basic groundwork, not only for the theoretical advantages that were afforded by operating gas chromatographic columns at high velocities (and hence high pressure), but the unique solvent-like characteristics these gaseous (fluid) mobile phases took on under tremendous pressure.

I became involved under the watchful eye of Giddings' research collaborator, Marcus Myers, in conducting solute migration studies at pressures up to 2000 atmospheres using carbon dioxide as the mobile phase. In those days, no columns existed that were packed to withstand such enormous pressures; likewise all of the experimental equipment had to be designed and fabricated from scratch. With the help of my colleagues, we overcame the barriers to working under such adverse conditions, but this was not without considerable pain and suffering in a figurative sense. The result was my first coauthored publication [1] entitled, "Dense gas chromatography at pressures to 2000 atmospheres".

In this publication, we had made differential migration experiments for simple solutes dissolved in what would later become known as supercritical carbon dioxide (SC-CO_2), and related the shift in chromatographic retention factors with pressure, to the changing 'solubility parameter' of the carrier gas. At 2000 atmospheres, carbon dioxide was beginning to show the solvency characteristics of moderately polar organic liquid solvents. Attempts at migrating or solubilizing macromolecular solutes, such as long-chained alkanes, various synthetic polymers, and proteins were partially successful. In today's light, these experiments would complement developments in a parallel field, supercritical-fluid extraction (SFE). However, the use of the Hildebrand's 'solubility parameter concept' explained the qualitative trends we saw in our data and rather fascinated me, as it did many chromatographers. I would make use of this concept almost 20 years later, as I will comment on shortly.

After a brief stint in industry, I resumed my graduate studies under two excellent mentors, Barry Karger at Northeastern University, and Dan Martire at Georgetown University. Research under these two mentors in physico-chemical surface and solution thermodynamic measurements by gas chromatography cemented by a physical chemistry approach to the separation sciences which had begun under Giddings. Unlike most of Karger's students who were involved in HPLC and capillary electrophoresis, my

research involved making sorption isotherm and precise retention volume measurements by GC using water, a rather unusual stationary phase [2]. As it turned out, I would revisit water over 25 years later in a slightly altered form.

From 1976 to 1986, I worked at several industrial positions as a separations specialist doing proprietary research that involved considerable use of GC, HPLC, and the development of process methodology. One memorable aspect during this time in my career was my involvement at Arthur D. Little, Inc. in Cambridge, MA in a venture development team that later became the nucleus of Critical Fluid Systems, Inc. The company purchased a crude SFE system that I had developed as an Assistant Professor in academia for their initial extraction studies. The design template for this apparatus would be repeated many times in slightly altered formats by many researchers and companies, resulting eventually in a hybrid system known as the Spe-ed unit [3] offered by Applied Separations, Inc. of Allentown, PA.

In 1986, I joined the Agricultural Research Service Northern Regional Research Center in Peoria, IL, where my interest and passion in supercritical fluid technology was rekindled. USDA had been exploring the use of supercritical fluids, such as SC-CO_2, as an alternative solvent media, to replace hexane as an extraction solvent. Research by John Friedrich at the Peoria laboratory had shown that at high pressures and temperatures, SC-CO_2 could readily solubilize significant quantities of vegetable oil from seeds, and lead to quick and efficient extractions in an environmentally benign matter [4]. I took up the charge of working in this area invoking the solubility parameter concept as I had done under Giddings to explain the salient features of oilseed solubility in supercritical fluid media [5]. However in 1988, I was approached by a sister agency, the Food Safety and Inspection Service (FSIS) regarding the possibility of using SC-CO_2 extraction to replace organic solvents for the extraction of lipid phases from meat products for pesticide residue analysis. This proved to be an ideal opportunity for transferring our processing methodology down to an analytical scale and to reduce the analyst's dependence on organic solvents for sample preparation. This transfer of critical fluid technology from process application to analytical use, and vice versa, has been a seminal theme in research conducted under my direction over the past 11 years.

Commensurate with the above, development was the first offering of capillary SFC systems by the Lee Scientific Company of Salt Lake City, UT. I convinced USDA to purchase one of these chromatographs on the basis that we just might be able to detect pesticide residues via flame ionization detection (FID), and that SFC could help define some of the physico-chemical parameters vital to achieving optimum results in SFE. It also turned out that SFC is a quick and efficient tool for the separation of many different types of lipid species; hence the technique has been used for the last decade to support our process SFE program as an analysis tool [6]. I became intrigued as to how the separation mechanism of SFC worked and eventually wrote a paper entitled, "Fundamentals and applications of supercritical-fluid extraction in chromatographic science" [7], and which has been widely cited ever since. This paper invoked the solubility parameter theory coupled with Flory-Huggins solution theory to offer a plausible explanation of the retention trends observed in capillary SFC.

By the early nineties it was apparent that simple analytical SFE was not a panacea for all of the sample preparation woes facing the analyst. It occurred to me about

this time that there might be some advantage in coupling SFE with a crude form of sorbent chromatography to allow in-situ cleanup of the resultant SFE extract. I reasoned by analogy that if the pesticide residue analyst could use non-polar eluents with tempered surface activity sorbents, that a form of supercritical fluid 'normal' phase chromatography could provide the same function. I believe that we were probably the first research group to demonstrate this principle [8], but many other researchers eventually took up the method. Today, both on-line and off-line use of sorbent beds in analytical SFE are routinely used for environmental, food, and drug analysis.

A fortunate and productive collaboration with Marvin Hopper of the FDA's Total Diet and Pesticide Research Center in Lenexa, KS, led to some other developments in analytical SFE that are based on chromatographic principles. Hopper had been using for some time a diatomaceous earth sorbent called Hydromatrix for liquid phase cleanup of extracts prior to pesticide residue analysis. This material was not unlike the early packed column GC support materials. Utilizing this as a sample matrix dispersant as well as extraction cell filler facilitated very efficient SFE of a variety of different types of food matrices. Eventually a USA patent [9] was issued to the author and Mr. Hopper for this development, and the material is widely used in many laboratories.

The experience with Hydromatrix and like sorbents only wetted my appetite to see how other sorbents faired in the presence of dense SC-CO_2. Since SC-CO_2 was not the best solvent for polar molecules, I reasoned that there might be some advantage in looking at the separation process in a different light; perhaps one could remove unwanted coextractives obtained in the total extract from polar target analytes. Because I was aware of the research studies of polymer researchers using gas chromatography to determine solute–polymer interactions in molten polymers (i.e., 'inverse' GC), I coined the term 'inverse' SFE [10] to characterize the above process. Due to circumstances beyond our control, we did not fully exploit this principle, but others filled the void and it has proven particularly facile for the analysis of drugs and active principles in pharmaceutical formulations.

Inverse GC, or using gas chromatography for physico-chemical measurements, has played a key role in my career since graduate school. I have authored or coauthored papers that have investigated solute probe interactions with volatile stationary phases, such as water and carbon tetrabromide, molten sulfur, and polystyrene above its glass transition temperature, and recently, vegetable or seed oils as stationary phases. The last study, along with research characterizing sorbent resins by injecting sorbate probes, has been completed to support concurrent studies in analytical and process SFE. One noteworthy citation [11], often ignored by others studying high pressure adsorbate–adsorbent interactions, correlated sorbate breakthrough volume trends with molecular interactions at the gas–solid interface. Further studies in our laboratory using gas–solid chromatography to study the effect of carbon dioxide versus other carrier fluids, on solute breakthrough volumes and adsorption coefficients, have shown that CO_2 substantially reduces retention volumes on many common analytical sorbents relative to helium and more 'ideal' fluids. Thus, CO_2 even close to ambient conditions, behaves in a non-ideal manner through increased gas phase interactions (i.e., second mixed virial coefficients) with solutes and its ability to displace sorbates from sorbent surfaces.

The above technique can be used to mimic the behavior of high pressure gas-adsor-

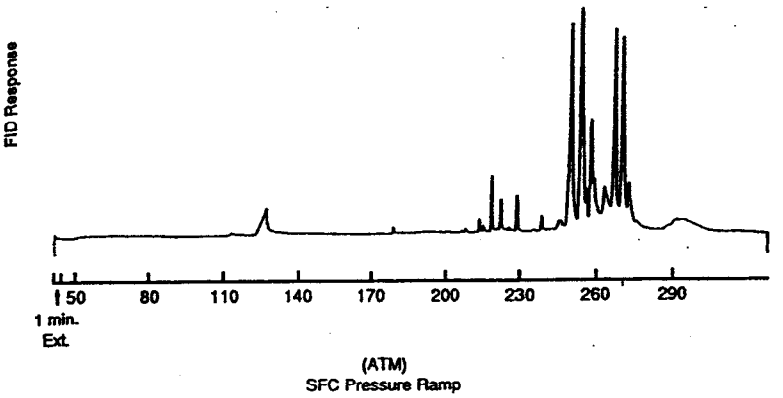

Fig. 1. SFE–SFC separation of the on-line CO_2 extract from a single dried-fruit beetle (live specimen).

bent systems such as those that occur in SFE schemes. Utilizing a modified inverse GC approach, we measured breakthrough phenomena for selected odoriferous probe molecules that mimicked components we wanted to remove from a recycle SC-CO_2 in our pilot plant operations at NCAUR (USDA's Northern Regional Research Center became the National Center for Agricultural Utilization Research in the early 1990s through an Act of Congress). The derived data permitted an estimate to be made on the effective service lifetime of sorbents, such as activated carbon, for purifying the SC-CO_2, recycled back into the extraction vessel.

Returning to our use of chromatography with supercritical fluids, we have practiced both open tubular and packed column SFC techniques. Although most of our studies have employed capillary SFC, we have also found niches for the packed column mode, and find arguments by proponents for one technique over the other, rather immature. I believe that one of the great benefits to using analytical SFC that often goes untouted, is its elimination of sample cleanup techniques that normally must be performed prior to GC. The versatility of pressure or density programmed SFC allows one to optimize a separation for the determination of target analytes, and to then 'program out' other species that interfere with the analysis. Capillary SFC also allows the establishment of signature profiles that can be used by analysts in product deformulation schemes. For certain specific micro-analysis problems, SFC can be combined with on-line SFE using small extraction cells. This principle is nicely demonstrated by the extraction of a live insect in a SFE cell with transfer of extract containing an active pheromone principle and cuticle lipids to a capillary SFC column (Fig. 1) [13].

A similar approach to the one described above was also developed for the on-line methylation of oils extracted from seeds in the extraction cell, prior to packed microbore SFC analysis. This early attempt was the beginning of a long association with the formation of fatty acid methyl ester (FAME) derivatives, not only for analytical purposes, but for process reaction chemistry in supercritical fluids. Several years ago we were asked to look into the feasibility of determining speciated fat levels in food products via FAME–GC analysis as mandated by the Nutritional Labeling and Education Act (NLEA). We developed a rather novel approach to this analytical problem

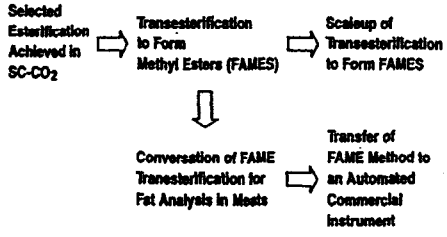

Fig. 2. Development and utilization of lipase reaction in SC-CO_2 at NCAUR.

by employing an enzyme (lipase) as an integral part of the extraction step, thereby facilitating the formation of the derivative after extraction with SC-CO_2, all in one step. The quantitative results were most gratifying and eventually the whole process was converted into an entirely automated scheme permitting SFE–SFR (supercritical fluid reaction) GC to be accomplished unattended overnight. This saga is nicely recounted in my Harvey Wiley Award address manuscript, and is amply described in Fig. 2.

Many of the principles learned from analytical supercritical-fluid chromatography have been incorporated into some of our processing schemes for fractionating or isolating high value chemicals from natural product matrices. For example, we have used a normal phase silica gel preparative chromatography step in enriching tocopherol extracts from a front end SFE step. Significant enrichments can be achieved to prepare solute-enriched extracts for the nutraceutical marketplace. Similarly, the same theme has recently been employed to isolate phospholipid-rich extracts, using an 'all-green' eluent consisting of pressurized SC-CO_2, ethanol, and water. Preparative and production scale SFC will play an increasing role in processing schemes employing critical fluids; the most obvious example being the new fish oil ethyl ester SFE-SFC plant in Tarragona, Spain.

No researcher is an island onto themselves and I have been aided over the years by my association with many excellent colleagues. One deserves special mention, Janet Snyder, who has shared her expertise on lipid analysis with me for the past decade. We have coauthored many analytical SFC publications together; but one not directly involving SFC, but rather SFE-GC, deserves special mention. We were asked on an emergency basis to explore the feasibility of using analytical SFE to determine the presence of contaminants from smoke in various items of produce that had been exposed to fire in a storage cave. The problem was daunting, since the compounds (aromatics) that would indicate such exposure were at the parts-per-billion level in meat and cheese products. Mrs. Snyder, with some advice from me, developed an excellent SFE-GC method that clearly showed, relative to background chromatograms, that the presence of such aromatic contaminants as naphthalene and ethylbenzene, were indicative of the food matrix being exposed to smoke and fire conditions.

As with many researchers in the field of chromatography, the use of tandem techniques has always been intriguing. Unfortunately analytical methods developed using hyphenated techniques are not always warmly received by the practicing analyst because of their complexity. For this reason, we have in recent years pursued off-line analytical SFE methodology as the methodology of choice, and the one that is most

likely to be adopted for routine use. However some of our earlier work and the efforts of others, has shown the SFE–SFC–GC, SFE–SFC–MS, and similar tandem techniques can fulfill a specific role. Our work has shown the SFC, both low and high resolution options, can be used to advantage for sample and extract cleanup, particularly in the field of trace toxicant analysis. Unpublished studies in our laboratory on using cross-linked polymer media (traditionally used for size exclusion chromatography), have revealed a better understanding of the fundamental basis on how these packing materials behave in the presence of supercritical fluids, in affecting solute separation. Interestingly, sight glass measurements have shown that highly cross-linked styrene/divinylbenzene resins do not swell in the presence of quite high pressure SC-CO_2, and that resultant separations are more the result of adsorption interaction of the solutes with the column packing than any molecular sieving effect.

Finally, an example of our research that indicates the value of a physico-chemical approach to chromatography or extraction, are studies on the effect of using binary supercritical fluids on solute solubility. Initial studies in this area were undertaken to answer the vexing question, does the presence of helium in SC-CO_2 reduce solute solubility in the compressed medium? The use of helium with SC-CO_2 had also been implicated in the instability of retention times in SFC and we were anxious to resolve the question. With the help of an excellent postdoctoral researcher, Zhouyao Zhang from Canada, we precisely measured the solubilities of several solutes in neat SC-CO_2, and SC-CO_2 containing a defined amount of helium in the cylinder. These solubility measurements were also accompanied by GC analysis of the binary gas mixture by traditional thermal conductivity detection and high pressure densitometer measurements of the density of the binary fluid mixture, both as a function of the time of use of the gas cylinder source. Our combined measurements definitely showed that helium in SC-CO_2 depressed solute solubilities.

After pondering this result for sometime, I decided that, if this were a general phenomena (and it is!), it might be put to good use in achieving more selective analyte extraction in SFE. Hence I instructed Zhang to try various mixtures of nitrogen with SC-CO_2 at different extraction pressures and temperatures to see if he could obtain a lipid-free extract from a food matrix (poultry peritoneal fat containing pesticide residues). Indeed, the suppression of the lipid solubility that we had seen in our initial solubility studies held in this case and we obtained an extract that could be used directly for GC-electron capture detection analysis of pesticide residues. Over the last year we have built several devices for generating these binary fluid phases and are using them not only in our analytical SFE research, but to generate binary fluid mixtures of utility in conducting reaction chemistry (i.e., hydrogenation) in supercritical fluid media.

31.I.1. In summary

I believe that the astute scientist should always be aware of the technology transfer possibilities in the research that she/he is developing. This is true whether one is considering SFC to SFE or vice versa, or conveying useful results from analytical to process application. The techniques and results developed in one form of chromatography may

have implications in similar separation techniques, be they small (analytical) or large (engineering) in magnitude. These rules have guided my approach to research over the years and provided gratifying extensions to my career in chromatography and separation science.

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Source: Chromatography: A Century of Discovery 1900–2000, the Bridge to the Sciences/Technology. Edited by Charles W. Gehrke, Robert L. Wixom, and Ernst Bayer. Journal of Chromatography Library, vol. 64 (New York, Elsevier) ISBN 0–444–50114–2 Chapter 5, Part D.31. Jerry W. King, p. 309 and Part 31.I. "The Use of Supercritical Fluids in Analytical Chemistry, p. 310–316. 2001